REMARKS

In the Office Action mailed July 22, 2005, Claims 1, 2, 5-17, 24-37, 39-66, 72-87, 94-107, and 109-133 were pending for consideration in the present application. All of such claims were rejected under 35 U.S.C. § 103(a) as allegedly obvious in view of one or more cited references. It is respectfully requested that the Examiner further consider the application in view of these remarks.

Rejections Under 35 U.S.C. § 103

The Examiner has rejected claims 1, 2, 5-17, 24-37, 39-66, 72-87, 94-107, and 109-133 as being allegedly unpatentable over U.S. Patent No. 5,922,355 (hereinafter "Parikh"). The Applicant respectfully submits that these claims are patentable over the cited reference for the reasons set forth below, and that the rejection should be withdrawn.

Before discussing the obviousness rejections herein, it is thought proper to briefly state what is required to sustain such a rejection. The issue under § 103 is whether the PTO has stated a case of *prima facie* obviousness. According to the MPEP § 2142, the Examiner has the burden and must establish a case of *prima facie* obviousness by showing the prior art reference as modified, or references combined, teach or suggest all the claim limitations in the instant application. Further, the Examiner has to establish some motivation or suggestion to combine and/or modify the references, where the motivation must arise from the references themselves, or the knowledge generally available to one of ordinary skill in the art. The Applicant respectfully submits that the Examiner has not satisfied the requirement for establishing a case of *prima facie* obviousness in any of the rejections.

The Present Invention

The present invention, as recited in independent Claim 1, provides for a pharmaceutical formulation having an active agent and a pharmaceutically acceptable vehicle. The active agent is found in two fractions, a solubilized fraction and a solid particle fraction. The solid particle fraction and the solubilized fraction are both present in the pharmaceutically acceptable vehicle. The solid particle fraction represents from about 5 wt% to about 80 wt% of the active agent and the solubilized fraction represents from about 20 wt% to about 95 wt% of the pharmaceutical formulation. The presence of the active ingredient in both a solubilized form and a solid form is an important element to the current invention.

Likewise, independent Claim 74 of the present application teaches a pharmaceutical system for the administration of an active agent, which also requires that the active agent be present in both a suspended or solid particulate phase and a solubilized phase.

Rejection in view of Parikh

The Examiner has rejected Claims 1, 2, 5-17, 24-37, 39-66, 72-87, 94-107, and 109-133 as allegedly obvious in view of Parikh. Parikh teaches the preparation of microparticles using a combination of surface modifiers with a phospholipid (column 1, lines 60-65). The growth of such microparticles, as well as storage stability, can be controlled by adding a combination of surface modifiers with a phospholipid to a formulation.

The Examiner has argued that, because Parikh employs drugs that are poorly soluble, they remain solubilized to some extent while the majority remains suspended. The Examiner further argues that, because Parikh teaches various concentrations of surface modifiers to maintain particle size, it would have been obvious to prepare a pharmaceutical composition wherein the active agent is present as both particles as well as in a solubilized form by optimizing the amount of the surface modifier. The Applicants respectfully disagree with these assertions, for the reasons discussed hereafter.

The Examiner has alleged that it would be obvious to one of skill in the art based on Parikh to prepare the pharmaceutical composition of the present claims by optimizing the amount of surface modifier. This suggestion is apparently due to Parikh's teaching that the amount of the surface modifier may control particle sedimentation and particle size. There is nothing in Parikh to suggest, however, that the amount of surface modifier affects the solubility of the active agent. Rather, Parikh teaches that a combination of a phospholipid and one or more surface modifiers adsorb to the surface of drug particles to a) convert lipophilic to hydrophilic surfaces with increased steric hindrance/stability, and b) possibly modify zeta potential of surfaces with more charge repulsion stabilization (column2, lines 13-19). These teachings are applicable to solid particulates, not to a solubilized drug, and would thus not provide one of ordinary skill in the art any teaching or suggestion concerning solubilized active agents. Additionally, Parikh does not teach the use of a

surface modifier without a phospholipid, so any effects presented therein cannot be relegated simply to the surface modifier.

Parikh does suggest that some of the functions of the surface modifier may include maintaining particle size, increasing storage stability, minimizing sedimentation, etc. (see column 3, lines 50-63), however these functions exclusively relate to particulate substances, not solubilized drugs. A drug that is solubilized is dissolved and is thus, by its very nature, non-particulate. Any teaching of a surface modifier affecting a surface would naturally relate only to a particulate form of the drug. As such, the Applicants respectfully assert that Parikh does not teach each and every element of independent Claims 1 and 74.

Even assuming, *arguendo*, that one skilled in the art would achieve a formulation having two fractions using Parikh, nothing in this reference teaches or suggests the ranges claimed for each fraction. Though it is possible that upon suspension a particulate form of a poorly solubilized active agent may have a particulate fraction and a solubilized fraction, the proportions of these fractions as required by Claims 1 and 74 would not be taught or suggested. Additionally, it is apparent from much of the data presented in the specification that these fraction ranges have heightened dissolution and bioavailability effects. For example, FIG. 6 shows the blood concentration of isotretinoin for both the formulation in Example 13 and a commercial product, ACCUTANE®. As described in paragraph [0269] this commercial formulation has less than 10% of the isotretinoin solubilized and the Example 13 formulation has at least 20% solubilized. FIG. 6 shows the dramatic increase in isotretinoin blood concentration from the Example 13 formulation as compared to the ACCUTANE® formulation. FIGs. 7 and 8 show similar results for the fenofibrate formulations of Examples 14 and 15 (greater than 30% fenofibrate solubilized) as compared to a commercial formulation of fenofibrate (TRICOR®). These results indicate that the formulations of the present invention possess proportions of solubilized vs. solid fractions that have superior bioavailability and dissolution characteristics as compared to a mere suspension of a poorly solubilized drug. As such, merely suspending a poorly solubilized drug in solution does not necessarily achieve results as seen with the formulations of Claims 1 and 74. Thus the methods of Parikh would not necessarily produce a formulation having a soluble fraction and a particulate fraction within the claimed ranges.

Accordingly, Applicants respectfully submit that Parikh does not teach or suggest each and every element of the present invention. Moreover, the Applicants submit that the reference does not contain sufficient teachings or suggestions to motivate one of ordinary skill in the art to modify and apply such teachings in arriving at the present invention. Therefore, Applicants submit that the rejection of the present claims in view of the Parikh patent is improper and respectfully request that it be withdrawn. Additionally, claims 2, 5-17, 24-37, 39-66, 72-73, 75-87, 94-107, and 109-133 are narrower in scope than the claims from which they depend, and are thus considered to be allowable along with claims 1 and 74.

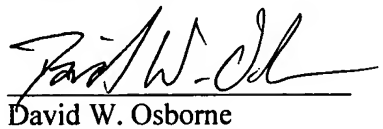
CONCLUSION

In view of the foregoing, Applicants believe that pending claims 1, 2, 5-17, 24-37, 39-66, 72-87, 94-107, and 109-133 present allowable subject matter and allowance thereof is respectfully requested. If any impediment to the allowance of these claims remains after consideration of the above remarks, and such impediment could be removed during a telephone interview, the Examiner is invited to telephone the undersigned attorney at (801) 566-6633 so that such issues may be resolved as expeditiously as possible.

Please charge any additional fees except for Issue Fee or credit any overpayment to Deposit Account No. 20-0100.

Dated this 22nd day of Nov, 2005.

Respectfully submitted,



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